DOCKET NO.: ISPH-0859USA

PATENT

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

On page 1, immediately after the title insert:

RELATED APPLICATIONS

This application is a US National Phase Application of PCT/US2004/026344 filed on August 12, 2004 which claims priority to US Patent Application Serial No. 10/641,455, filed August 15, 2003, which is incorporated herein by reference in their entirety.

SEQUENCE LISTING

A sequence listing is filed herewith in accordance with CFR 1.821 and is hereby incorporated by reference.

On page 29, lines 1-11:

Representative substituents groups of Formula I are disclosed in United States Patent 6,172,209, Application Serial No. 09/130,973, filed August 7, 1998, entitled "Capped 2' Oxyethoxy Oligonucleotides," hereby incorporated by reference in its entirety.

Representative cyclic substituent groups of Formula II are disclosed in United States Patent 6,217,358, Application Serial No. 09/123,108, filed July 27, 1998, entitled "RNA Targeted 2' Oligomeric compounds that are Conformationally Preorganized," hereby incorporated by reference in its entirety.

On page 29, lines 15-19:

Representative guanidino substituent groups that are shown in formula III and IV are disclosed in co-owned United States Patent <u>6,593,466</u> Application <u>09/349,040</u>, entitled "Functionalized Oligomers", filed July 7, 1999, hereby incorporated by reference in its entirety.

On page 29, lines 23-27:

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Representative dimethylaminoethyloxyethyl substituent groups are disclosed in International Patent <u>Publication WO 00/08044</u> <u>Application PCT/US99/17895</u>, entitled "2' ODimethylaminoethyloxyethyl Oligomeric compounds", filed August 6, 1999, hereby incorporated by reference in its entirety.

On page 31, line 19, to page 32, line 10:

Representative cytosine analogs that make 3 hydrogen bonds with a guanosine in a second strand include 1,3-diazaphenoxazine-2-one (R10 = O, R11 - R14= H) [Kurchavov, et al., Nucleosides and Nucleotides, 1997, 16, 1837-1846], 1,3-diazaphenothiazine-2-one (R10= S, R11 - R14= H), [Lin, K.-Y.; Jones, R. J.; Matteucci, M. J. Am. Chem. Soc. 1995, 117, 3873-3874] and 6,7,8,9-tetrafluoro-1,3-diazaphenoxazine-2-one (R10 = O, R11 - R14 = F) [Wang, J.; Lin, K.-Y., Matteucci, M. Tetrahedron Lett. 1998, 39, 8385-8388]. Incorporated into oligonucleotides these base modifications were shown to hybridize with complementary guanine and the latter was also shown to hybridize with adenine and to enhance helical thermal stability by extended stacking interactions(also see U.S. Patent Application Publication No US2003-0207804 entitled "Modified Peptide Nucleic Acids" filed May 24, 2002, Serial number 10/155,920; and U.S. Patent Application Publication No.US2003-0185906 entitled "Nuclease Resistant Chimeric Oligonucleotides" filed May 24, 2002, Serial number 10/013,295, both of which are commonly owned with this application and are herein incorporated by reference in their entirety).

On page 32, line 31 to page 33, line 3:

Further tricyclic heterocyclic compounds and methods of using them that are amenable to the present invention are disclosed in United States Patent Serial Number 6,028,183, which issued on May 22, 2000, and United States Patent Serial Number 6,007,992, which issued on December 28, 1999, the contents of both are commonly assigned with this application and are incorporated herein in their entirety.

On page 33, lines 24-35:

Further modified polycyclic heterocyclic compounds useful as heterocyclic bases are disclosed in but not limited to, the above noted U.S. 3,687,808, as well as U.S.: 4,845,205; 5,130,302; 5,134,066; 5,175,273; 5,367,066; 5,432,272; 5,434,257; 5,457,187; 5,459,255; 5,484,908; 5,502,177; 5,525,711; 5,552,540; 5,587,469; 5,594,121, 5,596,091; 5,614,617; 5,645,985; 5,646,269; 5,750,692; 5,830,653; 5,763,588; 6,005,096; and 5,681,941, and Unites States Patent Application Serial number 09/996,292 filed November 28, 2001 Publication No US 2003-0158403, certain of which are commonly owned with the instant application, and each of which is herein incorporated by reference.

On page 35, line 28, to page 36, line 2:

The oligomeric compounds of the invention may also be conjugated to active drug substances, for example, aspirin, warfarin, phenylbutazone, ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, carprofen, dansylsarcosine, 2,3,5-triiodobenzoic acid, flufenamic acid, folinic acid, a benzothiadiazide, chlorothiazide, a diazepine, indomethicin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic. Oligonucleotide-drug conjugates and their preparation are described in United States Patent 6,656,730 Application 09/334,130 (filed June 15, 1999) which is incorporated herein by reference in its entirety.